

In the claims:

1. (CURRENTLY AMNENDED) A method for identifying a therapeutically useful compound based on at least one functional SNP in a gene, said method comprising the following steps:

- a) Preselecting a candidate gene encoding a known polypeptide;
- b) Providing a sample population comprising a significant number of individuals chosen substantially at random from the general population without any selection criteria;
- c) Isolating from each individual of the sample population at least one fragment of the nucleotide sequence of the preselected candidate gene;
- d) Identifying at least one SNP in at least one fragment from at least one individual as obtained in step c); and
- e) From the SNP(s) identified in step d), identifying those whose presence in a gene

results in:

said gene encoding a polypeptide with a functionality selected from increased, reduced or suppressed biological activity;

increased, reduced or suppressed expression by said gene; or

at least one change in the biological activity of the polypeptide encoded by said gene, when compared to the functionality of a polypeptide encoded by said pre-selected gene without said SNP or the functionality of said pre-selected gene without said SNP, and whereby said therapeutic compound comprises said polypeptide encoded by said gene with the SNP identified in step e), or said gene with said SNP, or a molecule capable of functionally interacting with either of said foregoing polypeptide or gene.

2. (ORIGINAL) The method of claim 1, wherein the significant number of individuals chosen substantially at random in the population in step b) is greater than 100.

3. (ORIGINAL) The method of claim 1, wherein the genotype and/or the phenotype of individuals chosen substantially at random in the population in step b) are not known.

4. (ORIGINAL) The method of claim 1, wherein the fragment of the nucleotide sequence of the candidate gene is isolated in step c) by a PCR or RT-PCR reaction.

5. (ORIGINAL) The method of claim 1, wherein the identification of a SNP in step d) is carried out by at least one method selected from the group consisting of direct sequencing, multiplexing method using denaturing high performance liquid chromatography (DHPLC), single strand conformation polymorphism (SSCP), denaturing gradient gel electrophoresis (DGGE), methods based on the cleavage of the mismatch by chemicals or enzymes, allele-specific hybridization, allele-specific primer extension and allele-specific oligonucleotide ligation.

6. (ORIGINAL) The method according to claim 5, wherein the identification of at least one SNP in step d) is carried out by a multiplexing method using denaturing high performance liquid chromatography (DHPLC).

7. (ORIGINAL) The method according to claim 6, wherein the identification of at least one SNP in step d) is carried out by a multiplexing method using denaturing high performance liquid chromatography (DHPLC) followed by sequencing.

8. (CURRENTLY AMENDED) The method of claim 5, wherein the determination of the functionality of the SNP in step e) is carried out by at least one method selected among bioinformatic tools such as bioinformatic molecular modeling (~~in silico~~) and biological assay (~~in vivo or in vitro~~).

9. (ORIGINAL) The method of claim 5, wherein the determination of the functionality of the SNP in step e) is carried out by comparison of functionality between:

- i) a wild-type protein encoded by the reference wild-type nucleotide sequence of the preselected candidate gene, and
- ii) a mutated protein encoded by a mutated nucleotide sequence of the preselected candidate gene comprising at least one SNP as identified in step d).

10. (ORIGINAL) A method for determining at least one functional SNP in a gene, comprising the following steps:

- a) Preselecting a candidate gene;
- b) Providing a sample population comprising a significant number of individuals chosen substantially at random from the general population;
- c) Isolating from each individual of the sample population at least one fragment of the nucleotide sequence of the preselected candidate gene;
- d) Forming one or more mixtures comprising fragments isolated in step c) by randomly mixing fragments from one or more individuals;
- e) Conducting an analysis for comparing, between them, the fragments of each mixture formed in step d) in order to determine whether said mixture has a heterozygous or homozygous profile;
- f) Forming one or more homogeneous groups comprising at least one mixture analyzed in step e), each of said homogeneous group having an identical heterozygous or homozygous profile;
- g) Identifying at least one SNP in:
 - i) at least one fragment from each homogeneous group having a heterozygous profile formed in step f),
 - ii) at least one fragment of at least one mixture having an heterozygous profile as determined in step e), and/or
 - iii) at least one fragment isolated in step c) from an individual incorporated in a mixture having an heterozygous profile as determined in step e);
- h) From the SNP(s) identified in step g), identifying those with functionality.

11. (ORIGINAL) The method of claim 10, wherein the analysis conducted in step e) is carried out by a multiplexing method using denaturing high performance liquid chromatography (DHPLC).

12. (ORIGINAL) The method of claim 10, wherein the identification of a SNP in step g) is carried out by sequencing.

13. (ORIGINAL) The method of claim 10, further comprising the step of genotyping all or part of the nucleotide sequence of the preselected candidate gene identified as comprising at least one SNP.

14. (ORIGINAL) The method of claim 13, wherein said genotyping is carried out by minisequencing.

15. (WITHDRAWN) A method for the genetic diagnosis of a disease or a resistance to a disease linked to the presence of a mutated nucleotide sequence of the preselected candidate gene in an individual comprising detecting the presence or absence in said individual of at least one functional SNP identified by the method of claim 1.

16. (CURRENTLY AMENDED) A method for generating a map of genetic markers comprising the functional SNPs identified in at least one preselected candidate gene by the method of claim 1, comprising the following steps:

a) determining at least two functional SNPs by the method of claim 1 in at least one preselected candidate gene; and

b) organizing the functional SNPs determined in step a) one relative to the other according to their position on the nucleotide sequence of the preselected candidate gene and/or the relative position of the preselected candidate genes on a chromosome.

17. (WITHDRAWN) A method of preparing a polynucleotide comprising the nucleotide sequence of the preselected candidate gene comprising at least one functional SNP, comprising the following steps:

- a) Determining at least one functional SNP by the method of claim 1; and
- b) Producing a polynucleotide comprising a mutated nucleotide sequence of the preselected candidate gene comprising at least one functional SNP determined in step a).

18. (WITHDRAWN) A method of preparing a polypeptide comprising an amino acid sequence encoded by the preselected candidate gene comprising at least one coding functional SNP, comprising the following steps:

- a) Using at least one coding functional SNP determined by the method of claim 1; and
- b) Producing a polypeptide comprising a mutated amino acid sequence encoded by the preselected candidate gene comprising at least one coding functional SNP from step a).

19. (WITHDRAWN) A composition comprising a therapeutically effective amount of a polynucleotide prepared by the method of claim 17, and a pharmaceutically acceptable carrier.

20. (WITHDRAWN) A composition comprising a therapeutically effective amount of a polypeptide prepared by the method of claim 18, and a pharmaceutically acceptable carrier.

21. (WITHDRAWN) A method for treating an individual having a pathology and/or disease correlated to the presence or absence of a mutated allele comprising at least one functional SNP in a gene linked to said pathology and/or disease comprising administering a therapeutically effective amount of a polynucleotide prepared according to claim 17 and a pharmaceutically acceptable carrier.

22. (WITHDRAWN) A databank comprising functional SNPs determined by the method of claim 1.

23. (WITHDRAWN) A method for creating a databank of functional SNPs comprising performing the method according to claim 1, for at least one preselected candidate gene, and collecting said functional SNPs identified by said method.

24 (WITHDRAWN) A method for identifying the functional SNP(s) associated with at least one pathology and/or disease or the resistance thereto, comprising analyzing the databank of claim 22 for statistically relevant associations.

25. (WITHDRAWN) A method for treating an individual having a pathology and/or disease correlated to the presence or absence of a mutated allele comprising at least one functional SNP in a gene linked to said pathology and/or disease comprising administering a therapeutically effective amount of a polypeptide prepared according to claim 18 and a pharmaceutically acceptable carrier.

26. (ADDED) A method for identifying at least one SNP for developing a protein useful as an active ingredient in a medicament, said method comprising:

- a) Preselecting a candidate gene encoding a known polypeptide;
- b) Providing a sample population comprising a plurality of individuals chosen substantially at random from a general population;
- c) Isolating from each individual of the sample population at least one fragment of the nucleotide sequence of the preselected candidate gene;
- d) Identifying at least one SNP in at least one fragment isolated in step c); and
- e) From the SNP(s) identified in step d), identifying those whose presence in a gene results in:

said gene encoding a polypeptide with a functionality selected from increased, reduced or suppressed biological activity;

increased, reduced or suppressed expression by said gene; or

at least one change in the biological activity of the polypeptide encoded by said gene,

when compared to the functionality of a polypeptide encoded by said pre-selected gene without said SNP or the functionality of said pre-selected gene without said SNP, and
whereby said therapeutic compound comprises said polypeptide encoded by said gene with the SNP identified in step e), or said gene with said SNP, or a molecule capable of functionally interacting with either of said foregoing polypeptide or gene.

27. (ADDED) A method for identifying a therapeutically useful compound based on at least one SNP that affects a disease or resistance to a disease, said method comprising the steps of:

- a) Preselecting a candidate gene;
- b) Providing a sample population comprising a significant number of individuals chosen substantially at random from the general population without any selection criteria;
- c) Isolating from each individual of the sample population at least one fragment of the nucleotide sequence of the preselected candidate gene;
- d) Identifying at least one SNP in at least one fragment isolated in step c); and
- e) From the SNP(s) identified in step d), identifying those whose presence in a gene

results in:

said gene encoding a polypeptide with a functionality selected from increased, reduced or suppressed biological activity;

increased, reduced or suppressed expression by said gene; or

at least one change in the biological activity of the polypeptide encoded by said gene,
when compared to the functionality of a polypeptide encoded by said pre-selected gene without said SNP or the functionality of said pre-selected gene without said SNP, and

whereby said therapeutic compound comprises said polypeptide encoded by said gene with the SNP identified in step e), or said gene with said SNP, or a molecule capable of functionally interacting with either of said foregoing polypeptide or gene.